3 Connective tissue disorders

3.1 Analysis of Raynaud’s phenomenon in an infant and teenage population

ML GÁMIR, MJ RUBIRA, CM VAZQUEZ, M RIVENGA, R HORTA

Rheumatology Service, Hospital Ramón y Cajal, Madrid, Spain

Objective—To analyse the onset and evolution patterns as well as the prognostic value of Raynaud’s phenomenon (RP) in a cohort of children diagnosed and followed up in our paediatric rheumatology service.

Methods—Clinical variables (including those constituting the EULAR and ILAR criteria) and laboratory findings were registered longitudinally for each patient by paediatricians experienced in paediatric rheumatology. A database was constructed specifically for this purpose. In this study clinical findings and laboratory data from the first 6 months (for certain variables also for the first 12 months) were considered.

Results—322 patients qualified for classification according to the ILAR criteria. Of those 31/322 (10%) children were diagnosed only according to the ILAR criteria. 15% of the patients did not fulfill ILAR criteria for any of the categories and 6% fulfilled criteria for more than one category. As an example of the effect of different classification systems in our study, 160/322 were classified as oligoarticular by ILAR criteria and 191 by EULAR criteria.

Conclusion—The sensitivities for all sets except for the SEA six months. The initial fulfilment of the criteria was highly sensitive for all sets except for the SEA six months.
first concerns referred to by the adolescents were the side effects of steroid treatment (obesity and short stature), the difficulty of the daily use of solar protectors, the limitation on physical activity, the dietary restrictions, how to talk about the disease to friends and relatives, and the constant need for examina-
tion, laboratory tests, and, eventually, for invasive procedures (biopsies). The adolescents re-
quested information about the disease itself, its treatment, and the possibility of cure, pregnancy, and contraceptive use. The au-
thors emphasise the importance of the meth-
ology with groups of adolescents with SLE, in which the partner works as a “mirror”—making the adolescents perceive themselves, and as a facilitator—helping them to identify their concerns, anxiety, and expectations. The group was shown to be effective in complementing medical assistance, promoting better adherence to the treatment and a better social and familiar environment through the explanation of sev-
eral aspects of the disease.

3.5 Neutropenia caused by anti-Ro autoantibodies in neonatal lupus

R CIMA*, H SCOFIELD†

*Paediatrics, ICP, Milano, Italy; †Oklahoma Medical Research Foundation, OK, USA

Background—Neonatal lupus (NL) provides a situation in which the pathogenicity of anti-
bodies can be evaluated. Transplacentally acquired anti-Ro (or SS-A) autoantibodies are found in the sera of babies with congeni-
tal heart block or other less common manifestations of NL, such as skin rash, liver disease, or haemocytopenia.

Case report—We report an infant, born to a mother with anti-Ro, who had profound neutropenia. A 30 year old woman with an undifferentiated connective tissue disease gave birth to a healthy girl. Laboratory tests performed on the baby at follow up, 10 weeks after birth, showed normal white blood count, but an absolute neutrophil count of 120/µl. Causes of congenital and acquired neutrope-
nia in the case of the girl, bone marrow aspirate did not show major abnormalities. IgG anti-
granulocyte antibodies were detected in the baby's serum. Fluorescence activated cell sort-
ing showed binding of mother’s and baby’s serum to intact neutrophils. To determine the specificity of this binding, purified 60 kDa Ro was used as inhibitor. After this treatment, the binding of each serum to the cell surface of neutrophils was drastically reduced. The specificity of binding was further studied in immunoprecipitation with enzyme-linked immunosorb-
ent assay (ELISA). When HeLa cell extract was used as antigen, sera of both the mother and child bound 48 kDa La but 52 kDa Ro was not bound. The 60 kDa Ro antigen was bound strongly by both sera in a direct antigen solid phase assay. Using nitrogen cavitination, we were able to detect the 60kDa Ro antigen was not bound. The 60 kDa Ro antigen was used as antigen, sera of both the mother and child showed a species purified neutrophil membranes and found that the mother’s and child’s sera bound a species at a predicted molecular weight of 64 kDa, recently recognised as a novel autoantigen in systemic lupus erythematosus and immunolo-

gically cross reactive with 60 kDa Ro. Such binding was in fact inhibited by incubation of sera with 60 kDa Ro.

Conclusions—Our results show that anti-Ro can directly lower the neutrophil count by binding the cell surface of neutrophils.

3.6 Laboratory markers of endothelial damage in the assessment of the activity of childhood rheumatic diseases

P DOLEZALOVA, P TELEKESOVA, D NEMCOVA, J HOZA

Department of Paediatrics and Adolescent Medicine, Charles University in Prague, 1st Faculty of Medicine

Various laboratory markers of endothelial cell damage/activation seem to play an important part in rheumatic disease pathogenesis. Among these we have chosen factor VIII related antigen (FVIII:Ag), platelet soluble forms of vWF and circulating adhesion molecule concentrations. To answer this question we examined children with different types of rheumatic diseases. Factor VIII related antigen was found in the sera of babies with congenital heart block. In addition, in children with JIA the highest values of the vWF were observed. vWF reached the highest levels in patients with SLE (mean (SD) 159.9 (24.3)%), p=0.05, whereas the child with SLE and NL had 87% of the reference limits in 77.8% of patients with JIA and 82.4% of patients with SLE. We found a significant tendency for both ICAM-1 and E-selectin to decrease with age (p=0.01). ICAM-1 reached the highest values in the VAS group (428.4 (113.4) ng/ml) and JIA-poly (376.51 (22.6) ng/ml) groups (p=0.05). Patients with acute HSP did not differ significantly from controls. In the JIA-poly group E-selectin also showed significant increase (444 (82.7) ng/ml, p=0.05). All patients in this group had clinically active disease; its duration and current treatment did not have any signifi-
cant impact. No signs of secondary vasculitides were seen and there were only 2 patients with systemic onset JIA. High adhesion molecule values could be a consequence of generalised endothelial activation followed by their non-
specific release. Platelets are known to be hyperactive and highly vascular synovium in inflamed joints could be the main source of their production. To answer this question we exami-
ned 14 paired sera of sera and synovial fluid from patients with JIA and JIA related syndromes. Joint aspiration was indicated. Interestingly, we found no significant difference in ICAM-1 and E-selectin concentrations.

Conclusions—Our results show that anti-Ro can directly lower the neutrophil count by binding the cell surface of neutrophils.

www.amrheumdis.com

showed that the presence of damage was positively associated with the SLEDAI score (odds ratio (OR)=1.1, p=0.005), cumulative drug score (OR=1.0, p<0.001), and NPS disease at onset (OR=4.4, p=0.008) and negatively associated with Raynaud phenomenon at onset (OR=0.2, p=0.01).

**Conclusions**—Our results show that permanent damage is common in paediatric onset SLE and is significantly associated with lupus disease activity and cumulative drug treatment. NPS disease at onset is a strong predictor of late damage, whereas the presence of Raynaud phenomenon may exert a protective effect.

### 3.9 Uncommon causes of liver disease in juvenile systemic lupus erythematosus

A RAVELLI, C MALATTIA, F TEMPORINI, S MAGNI MANZONI, C MORETTI, G ROSSI, I BASSI, A MARTINI
Departamento di Scienze Pediatriche, Università di Pavia, IRCCS Policlinico San Matteo, Pavia, Italy

**Background**—Severe liver disorders are rare in patients with systemic lupus erythematosus (SLE). We report two patients with juvenile SLE who developed uncommon hepatic complications.

**Case reports**—Patient No 1: A 10 year old girl was admitted with a 3 week history of malar rash, intermittent arthritis, fatigue, and abdominal pain. Physical examination showed haemolytic anaemia, thrombocytopenia, and positive antinuclear antibodies (ANA) and anti-DNA antibodies. High titre antcardiolipin antibodies (aCL) and lupus anticoagulant (LA) were detected. A diagnosis of SLE was established. During a stay in hospital the girl developed enlargement of the liver, which was tender at palpation. Ultrasonography showed a large thrombosed splenic vein along the lumen of the inferior vena cava (Budd-Chiari syndrome). Based on the association of vascular thrombosis and positive antiphospholipid antibodies, antiphospholipid syndrome was diagnosed and long term anticoagulation treatment was started.

Patient No 2: A 9 year old girl, who had had autoimmune thyroiditis since the age of 6 years, was admitted with a 1 week history of fever, fatigue, arthralgia, and purpuric rash in the legs. Physical examinations showed hepatosplenomegaly, ascites, and oedema of the ankles. Laboratory investigations disclosed pan-cytopenia, liver transaminase increase, hypoprotinaemia, low serum complement levels, and positive ANA and anti-DNA antibodies. aCL and LA were absent. Liver ultrasonography showed an enlarged liver with diffuse pseudonodular changes. A percutaneous biopsy showed necrotising arthritis with nodular regenerative hyperplasia of the liver. A diagnosis of SLE with necrotising arteritis of the liver was established. A percutaneous liver biopsy showed necrotising arteritis with nodular regenerative hyperplasia of the liver. A diagnosis of SLE with necrotising arteritis of the liver was established. During a stay in hospital the girl developed enlargement of the liver, which was tender at palpation. Ultrasonography showed a large thrombosed splenic vein along the lumen of the inferior vena cava (Budd-Chiari syndrome). Based on the association of vascular thrombosis and positive antiphospholipid antibodies, antiphospholipid syndrome was diagnosed and long term anticoagulation treatment was started.

**Conclusion**—The reported patients demonstrate the proteinic clinical spectrum of liver disease in juvenile SLE.

### 4 Epidemiology and outcome

#### 4.1 Epidemiology of rheumatological diseases in Latvia

V STANEVICH, A KOKINA, R SHANTERE, A SHEGOLEVS
Medical Academy of Latvia

**Objective**—To research the epidemiology of rheumatic diseases in children and adolescents aged 1–18 years to obtain comparative data with those of other countries.

**Methods**—We used the children’s rheumatic diseases register data obtained by January 2000 to determine incidence and prevalence. **Results**—1251 children and adolescents aged 1–18 have rheumatic diseases. 70.4% have been diagnosed juvenile chronic arthritis (JCA), with prevalence 11.1/100 000 and incidence 34.3/100 000. 36% have registered oligoarthritis, 61% polyarthritis (rheumatoid factor positive 5.2%), 2% systemic form arthritis, 0.5% psoriasis with arthritis, 0.5% Cohn’s disease and ulcerous colitis with arthritis. Eye injuries in patients with JCA occur in 2.4% of cases. The prevalence of collagenoses is 11.1/100 000 and incidence 2.1/100 000. There was an increase of scleroderma with a prevalence 4.5/100 000. Since 1993 cases of rheumatic fever have increased, reaching a prevalence of 12.6/100 000 and an incidence of 2.1/100 000 in 1999. 49.3% have endocarditis. Epstein-Barr virus (9.8%) and streptococcal infection (8.6%) are common. **Conclusion**—Epidemiological data in children and adolescents with JCA and collagenoses are similar to those of the developed countries, except for the higher incidence of eye injuries in patients with JCA. Rheumatic fever with frequent valvular injuries has a comparatively higher occurrence. In 38% of patients the cause of acute arthritis is unknown.

#### 4.2 High prevalence of childhood chronic arthritis among the Shipibo people of Amazonian Peru

M ANDERSSON, S MYRNERTS, A HANSSON, A FASTH
Department of Paediatrics, University of Göteborg, Göteborg, Sweden

Few prevalence figures of childhood chronic arthritis exist for developing countries and even fewer for the indigenous population living a traditional life in those countries. We undertook a prospective population based study of the prevalence rate of childhood arthritis among the Shipibo people living in the Amazonian part of Peru.

**Methods**—As most adults and children are illiterate and time is vaguely defined as the number of elapsed rainy or dry seasons, no established criteria could be used. Instead a questionnaire was constructed with questions that aimed at differentiating between joint disorders of traumatic, infectious, and rheumatic aetiology. The questionnaire was given orally by an interpreter to all children present in the villages at time of the investigation and to a close adult relative. All children were physically examined for the presence of arthritis. The study area was Shipibo villages accessible from a smaller town and the study was performed during January and February 1999.

**Results**—651 of 785 children (83%) living in 6 areas of Yarina Cohca and 2 villages were examined personally by two of us and had the questionnaire filled in. 1% had joint complaints of traumatic cause, 1.4% of possible infectious origin, and 1.8% a possible rheumatic joint disorder. Of the 12 children with a possible rheumatic arthritis, 4 had active arthritis at time of investigation, which corresponds with a prevalence of 614 per 100 000 children <16 years of age. If all 12 children with a possible arthritis are included the prevalence is 1843 per 100 000 children <16 years of age. This very high prevalence must be viewed with caution as the study period was short, the most remote part of the Shipibo area could not be accessed, the concept of medicine is traditional, and longstanding reactive arthritis might have been included. This means that the prevalence as well as possibly being overestimated might even have been underestimated. Also among adults of the Shipibo people a very high prevalence, close to 10% has been reported, indicating that the prevalence of chronic arthritis among children also may be high.

#### 4.3 Adaptation and application of childhood health assessment questionnaire (CHAQ) to an indigenous population of Amazonian Peru

S MYRNERTS, M ANDERSSON, A HANSSON, A FASTH
Department of Paediatrics, University of Göteborg, Göteborg, Sweden

The CHAQ has been successfully adapted and applied to most industrialised societies and also to a country in transition like Costa Rica. Common to all those countries is a high educational level. We attempted to determine whether it was possible to adapt the Costa Rican version of the CHAQ (CR-CHAQ) to the conditions and language of the Shipibo people, a well defined indigenous group living a traditional life in the Amazonian part of Peru.

**Method**—A cultural adaptation and linguistic translation of certain key parts of the CR-CHAQ was done. It was tested on children and parents without joint disorders and was with minor alterations well understood. Self administration was not possible, however, as most adults and children cannot read or write. Instead an interpreter gave the Shipibo-CHAQ (SH-CHAQ). The SH-CHAQ was tested on 12 children with possible rheumatic joint disorders, and a close adult. For children below 10 years of age, the SH-CHAQ was applied only to the adult.

**Results**—Cross cultural validity: Most questions had to be adapted to Shipibo lifestyle and traditions. The children gave higher disability scores than the adults. Test-retest reliability was found between the disability index for the first and second application both for children and adults. The correlation for children ( Spearman’s correlation coefficient =0.994, p<0.002) was higher than that for the adults ( r=0.839, p<0.02). Inter-rater score correlation: No correlation was found between the disability index for children and adults at the first application, but the second application showed a good correlation ( r=0.975, p<0.02). The difference between the first and second application might be due to exaggeration by parents who expected to obtain health care if the child was more severely ill.

**Conclusion**—By carefully analysing the CHAQ and adapting the questions to the Shipibo culture we could successfully apply the new SH-CHAQ with a high test-retest and interobserver reliability.

#### 4.4 Remission in juvenile chronic arthritis: a cohort study of 683 consecutive cases

C ARNOLDI, V GERLONI, M GATTINARA, E LUPI, F FANTINI
Chair of Rheumatology of the University of Milan, Centre for Rheumatic Children, Gaetano Pit Institute, Milan, Italy

Evaluation of the prognosis of the juvenile forms of chronic arthritides is difficult because most patients are lost at follow up when they reach adulthood. Our institute is a privileged observatory as it is open to both juvenile and adult patients, so that children do...